REMARKS

Claims 21-26, 34-38 and 40 are under prosecution. Applicants acknowledge the election of the fore-mentioned claims and thus cancel claims 1-20, 27-28, 30-33 and 41-62 as non-elected claims. Claim 21 has been amended to better claim the subject matter that Applicants regard as the claimed invention. Claims 23, 24, 26, 34, 37, and 38 have been amended for improved clarity. None of the amendments made herein constitutes the addition of new matter.

Objections to the Specification:

The disclosure was objected to because of the informalities. With the entry of this Amendment, the inadvertent typographical error of "inactivated PT8 virus" has been corrected to be "inactivated PR8 virus" on page 6, line 18.

Claim Rejections under 35 U.S.C. §112:

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants respectfully traverse this rejection.

The Office Action alleges that the phrase, "a sialic acid binding component" in claim 21 is vague and indefinite. Applicants submit that this is a well known and commonly used phrase in the art. A person of ordinary skill in the art readily understands this phrase as a component such as hemagglutinin (HN) that binds sialic acid. Withdrawal of this rejection is respectfully requested.

Claims 21 and 38 are alleged to be unclear based on the recitation of "an inactivated or attenuated target cell or virus". Applicants point out that this phrase is specifically defined as a target tumor or cell which does not cause a tumor or disease in a human or animal to which it is administered. The allegation that the accepted meaning of this phrase is a died (dead?) cell after chemical or physical treatment is not correct. The

types of treatments described in the Specification, i.e., heat, formalin, beta-propiolactone treatment or serial passage make the target cell or virus non-tumorigenic and replication defective. Applicants submit that the recited phrase is used within the art-recognized meaning and thus claims 21 and 38 as filed are clear to one of ordinary skill in the art.

Claim 23 is alleged to be vague and indefinite based on the recitation of the term, " preparation". Without acquiescing to this rejection and in the interest of advancing the prosecution of this application, claim 23 has been amended to delete this term. Thus, amended claim 23 is deemed to be clear and definite. Withdrawal of this rejection is respectfully requested.

Claim 24 is alleged to be unclear based on the usage of the term, "sialic acid containing virus preparation". Without acquiescing to this rejection, claim 24 has been amended for improved clarity.

Claims 24 and 38 are alleged to be indefinite because of the term, "virus like particle". It is submitted that this term is well known and commonly used in the art. Virus like particle (VLP) refers to a particle that resembles a given virus with respect to the size and structure but without the infectability.

Claim 25 is alleged to be indefinite because of the term, "an enveloped virus". A person of ordinary skill in the art readily understands that the enveloped virus refers to the viruses whose nucleocapsid is surrounded by an envelop that usually has a lipid bilayer component derived from a modified host cell membrane plus a projecting outer layer of glycosylated proteins (see Medical Microbiology, 3rd Ed. Edited by Baron S. Churchill Livingstone, New York, p559, under the heading of Structure and Function). Furthermore, specific examples of the enveloped virus useful for the claimed invention are provided as HIV, SIV, FIV and others, on page 4, line 27 in the Specification.

In summary, based on the foregoing, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

Claim Rejections under 35 U.S.C. §112:

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §112, first paragraph, based on the allegation that the Specification does not provide enablement for making an immunogenic composition comprising any or all sialic acid binding component and any or all inactivated or attenuated tumor cell, virus or bacterial cell that can produce the same immune response against any or all specific antigens from said any or all inactivated or attenuated tumor cell, virus or bacterial cell. Applicants respectfully traverse this rejection.

The claimed invention is an immunogenic composition useful for providing immune protection in a subject deficient in CD4+ T cells. This invention was based on the inventors' new discovery that the sialic acid-containing vaccine compositions administered together with a sialic acid binding composition, as specifically exemplified by a formalin-inactivated influenza virus composition, did elicit protective immune response in a CD4+ T cell independent manner. The inventors of the present application are the first to make this discovery.

The office Action alleges that the claimed invention is unpredictable based on the studies of Miotti et al. This allegation is not justified in the present case. Miotti et al. reported that there is no increase in the magnitude of antibody response after the second dose of inactivated influenza virus vaccine in their studies in which a two-dose regimen of vaccine was compared with a single-dose regimen in inducing protective antibody responses. Based on these results, Miotti et al. speculated that a substantial portion of individuals with symptomatic HIV infection might remain unprotected from influenza, even after immunization with a two-dose regimen. The relevance of the Miotti et al. reference to the claimed invention is not clear to the Applicants. There is no teaching therein that an immune composition containing sialic acid binding component and sialic acid containing component can provide immune protection in a CD4 T cell independent manner.

The office Action alleges that the Specification does not provide working examples of a composition comprising sialic acid binding component or sialic acid containing viral preparation in combination with an inactivated or attenuated target virus such as HIV.

Applicants submit that the Specification provides a specific example of the claimed invention using a formalin-inactivated influenza virus composition in mice, C57BL/6-Cd4$^{tm/mak}$ that had a targeted disruption in their CD4 gene and thus lacked functional CD4^{+} T cells. The level of the skill in the relevant art is high and the necessary techniques to make the claimed invention are readily available. Therefore, it is submitted that a person of ordinary skill in the art can make and use the invention as claimed, based on the disclosure in the present application combined with the knowledge available in the art.

Claim Rejections under 35 U.S.C. §102:

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Compans (US Patent No. 4,790,987). Applicants respectfully traverse this rejection.

The claimed invention is an immunogenic composition containing sialic acid which when administered with a sialic acid binding component provides protective immunity in a CD^{+} T cell independent manner and thus particularly useful for AIDS and ARC in humans and other similar immune compromised conditions.

The cited patent teaches vaccine compositions useful for virus-caused diseases by using the immunogenic viral envelope glycoprotein complexed with a lipid. This reference defines the composition to contain the fusion and/or receptor binding viral envelop glycoprotein. The cited reference does not teach sialic acid containing immunogenic compositions or a sialic acid binding component. Thus, a person of

ordinary skill in the art cannot make the claimed invention based on the teachings of Compans.

Claims 21-25 and 34-38 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Pertmer et al. (J. of Virol. 1996 Vol.70: 6119-6125). Applicants respectfully traverse this rejection.

Pertmer et al. compared the results of DNA vaccination by two modes of administration and reported that the types of responses elicited following DNA immunization are dependent on both the identity of the antigen and the route of DNA administration. The Pertmer et al. reference does not teach the claimed invention. Nothing in the cited reference teaches the immunogenic composition containing no sialic acid or sialic acid binding component. Pertmer et al. uses DNA vaccination method not an inactivated or attenuated target cell or virus. Therefore, the claimed invention cannot be anticipated by Pertmer et al.

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Muster et al. (J. Virol. 1994 Vol.68:4031-4034). Applicants respectfully traverse this rejection.

Muster et al. describes an epitope derived from gp41 of HIV type 1 and antibodies specific for the epitope elicits cross-neutralizing activity against other related HIV isolates. Muster et al. does not mention the immunogenic composition containing sialic acid and a sialic acid binding component. There is no teaching in this reference that such an immunogenic composition works in a CD4 T cell independent manner.

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Pales et al. (J. Inf.Dis. 1997 Vol.176: S45-S49). Applicants respectfully traverse this rejection.

Pales et al. is a general reference that discusses various ways of developing more effective influenza virus vaccines by cold adaptation or introducing mutations. This reference does not teach the claimed immunogenic composition.

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Li et al. (J. Virol. 1993 Vol. 67:6659-6666). Applicants respectfully traverse this rejection.

Li et al. describes the use of chimeric influenza virus expressing an epitope of gp120 of HIV-1 to induce neutralizing antibodies. There is no mention of the sialic acid containing composition or the sialic acid binding component.

Claims 21-26, 34-38, and 40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Chiba et al. (Arch Virol. 1999 Vol.144:1469-1485). Applicants respectfully traverse this rejection.

Chiba et al. reports that recombinant vaccinia viruses expressing an HIV-1 glycoprotein epitope in the context of an influenza hemagglutinin cassette primed epitope specific CD8 positive cytotoxic T lymphocytes. This reference does not appear to be relevant to the claimed invention. There is no teaching of an immunogenic composition containing sialic acid nor an inactivated or attenuated target cell/virus in this reference.

Anticipating references must teach each and every element of the claimed invention. MPEP 2131. The claimed immune composition contains sialic acid and a

component having sialic acid binding properties, which provides protective immune response in a $CD4^+$ T cell independent manner. The claimed invention is particularly useful for the immune comprised conditions in which the $CD4^+$ T cells are depleted such as AIDS, ARC and the like. None of the cited references teach the claimed invention. Applicants submit that the claimed invention is not anticipated by the cited references and the rejection under 35 U.S.C. §102 be withdrawn.

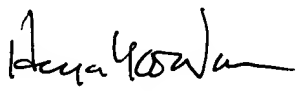
Conclusion

Based on the foregoing amendments and remarks, it is submitted that this case is deemed to be in condition for allowance and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of $200.00 as required under 37 C.F.R. 1.17(a)(2) for a small entity. If the amount submitted is incorrect, however, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



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In the Specification:

Please replace the fifth paragraph on page 2, starting in line 30 and continuing to page 3, with the following.

Through cognate interaction between antigen specific B cell and CD4 αß T cells, the $CD4^+$ αß T cells secrete cytokines that initiate the immunoglobulin class switching process from IgM to IgG (Parker, D.C. (1993) *Annu. Rev. Immunol.* 11:331; Finkelman et al. (1990) *Annu. Rev. Immunol.* 8:303; and Snapper, C. M. and Mond, J. J. (1993) *Immunol. Today* 14:15). These T cell dependent antibody responses are accompanied by the formation of germinal centers of B cells in the lymphoid organs such as the spleen and lymph nodes. Recent studies have shown that Ig class switching can also be induced in T cell deficient mice when infected with live viruses (Maloy et al. (1998) *Proc. Natl. Acad. Sci. USA* 95:1160; Szomolanyi-Tsuda, E. and Welsh, R. M. (1996) *J. Exp. Med.* 183:403; and Szomolanyi-Tsuda et al. (1998) *J. Virol.* 72:6665). When T cell deficient mice (T cell receptor β chain knockout [TCRβ-/-] or T cell receptor α chain knockout [TCRα -/-] were infected with live polyoma viruses, a protective, virus-specific IgG response was reported in the absence of helper T cells. However, virus-like particles and soluble capsid antigens (VP1) were reported not to induce detectable IgG responses. In studies with VSV, TCRα -/- mice were found to produce [product] neutralizing IgG antibodies when infected with live VSV or with a recombinant vaccinia virus expressing the VSV glycoprotein (Maloy et al. (1998) *supra).* These results suggest that there may be alternative mechanisms for antibody class switching and induction of IgG responses.

Please replace the third paragraph on page 6, lines 17-25 with the following.

FIG 1: Magnitude and isotype profiles of serum antibody responses to intramuscular immunization with inactivated PR8 [PT8] virus in $CD4^+$ T cell deficient and immunocompetent mice. 16 week old $CD4^+$ T cell deficient mice or C57B/6 mice were immunized intramuscularly with 10μg/mouse of inactivated PR8 virus, mice were boosted with the same dose after 15 days. Con: Control, unimmunized $CD4^+$ T cell deficient mice (n = 5). CD4KO: $CD4^+$ T cell deficient mice received inactivated [PT8] PR8 virus (n = 5). C57B/6: C57B/6 immunocompetent mice received inactivated PR8 virus (n = 5). First: Samples were measured 15 days after first immunization. Boost: Samples were measured 10 days after boost. Serum samples were assayed in 1:400 and 1:1600 dilutions. One experiment representative of two with comparable results is shown.

In the Claims:

21. (Once amended) An immunogenic composition useful for providing immune protection in a human or animal deficient in CD4+ T cells, comprising a sialic acid binding component and an inactivated or attenuated target cell or [an inactivated or attenuated target] virus.

23. (Once amended) The immunogenic composition of claim21 wherein said sialic acid binding component is comprised in an inactivated or attenuated [preparation of an] orthomyxovirus or paramyxovirus.

24. (Once amended) The immunogenic composition of claim 22 further comprising a virus like particle or an inactivated or attenuated [sialic acid containing] virus preparation containing sialic acid.

26. (Once amended) The immunogenic composition of claim 25 wherein said [is an inactivated tumor cell.] virus preparation is a preparation of simian immunodeficiency virus, human immunodeficiency virus, feline immunodeficiency virus, or bovine immunodeficiency virus, rabies virus, measles virus, vesicular stomatitis virus, flavivirus, alphavirus or herpes virus.

34. (Once amended) An immunogenic composition comprising a sialic acid binding component and [at least one] antigen of a target cell or target virus.

37. (Once amended) The immunogenic composition of claim 34 wherein the [at least one] antigen of a target cell or target virus comprises sialic acid or polymerized sialic acid.

38. (Once amended) The immunogenic composition of claim 37 wherein the [at least one] antigen of a target cell or target virus is comprised within inactivated or attenuated target cell or inactivated or attenuated target virus or virus-like particles of a target virus.